REMARKS

Claims 11, 20, 23 and 26 have been cancelled without prejudice or disclaimer of the subject matter contained therein. Thus, claims 1-10, 12-19, 21-22, 24-25 and 27-38 are pending. Claims 1, 4, 6-7, 12, 19, 21, 22, 24, 25, 27, 28, 31, and 33-38 have been amended as indicated above.

Rejections under 35 U.S.C. §112, second paragraph

The Examiner maintains several of the rejections under 35 U.S.C. §112, second paragraph for an asserted lack of clarity of the claims. Applicants will address each rejection in turn.

Claim 1 has been rejected as being unclear "because there appears to be a correlation step missing for the detection of the analyte. It is unclear how the analyte can be detected without the use of a label." Applicants traverse this rejection and withdrawal thereof is respectfully requested. Claim 1, as amended, recites that a method of determining an analyte in a sample comprising the steps of:

a) contacting the sample with an amount of a receptor which binds specifically to the analyte to form an analyte/receptor complex, and which is in excess of that required to bind all analyte in the sample,

b) isolating on a solid phase 0.001-50% of receptor contacted with the analyte, including analyte/receptor complex and unreacted receptor,

c) detecting the amount of analyte/receptor complex in said isolated receptor, and

d) from the detected amount of analyte/receptor complex, determining the concentration of analyte in the sample.

Step c) of claim 1 specifically recites detecting the amount of analyte/receptor complex in the isolated receptor and step d) recites from the detected amount of analyte/receptor complex, determining the concentration of analyte in the sample. Thus, claim 1 contains a "correlation" step, i.e. correlating the detected amount of analyte/receptor complex to the concentration of analyte in the sample. The Examiner is of the position that a "label" is necessary to perform steps c) and d). However, the Examiner has provided no basis for this position. In addition, the specification on page 6, lines 18-24 indicate that the detection reagent is usually labeled; however, it is also indicated that this method is not required. It will be readily appreciated by one skilled in the art that the detection step can be performed by any one of a number well-known methods. As such, the precise detection method used is not an essential feature of the invention and need

not be recited in the claims. Withdrawal of the rejection is respectfully requested.

Claim 1 has been rejected as being unclear in the recitation of "specified fraction." The claims have been amended to replace define the fraction in terms of "the ratio between said isolated fraction of receptor and receptor contacted with the sample is in a range of from about 1:2 to about 1:1000." Support for this amendment may be found on page 5, first paragraph of the specification, which states that the ratio of total binding capacity of analyte-specific receptor contacted with the sample (i.e. the total amount of receptor) and (i) the binding capacity of the receptor-binding ligand immobilized to the solid phase or ligand-binding capacity of the analyte-specific receptor (i.e. the fraction of receptor that will be immobilized) is from about 2:1 to about 1000:1. Thus, claims 1, 19, 22 and 25, have been amended to incorporate the subject matter of cancelled claims 11, 20, 23 and 26.

Claim 1 (d) has been rejected for lacking antecedent basis for "the concentration." Similarly, claims 33, 34 and 37 have been rejected for lacking antecedent basis for the terms "the receptor-binding capacity", "the analyte-specific binding capacity", "the ligand-binding capacity" and "the range." Applicants again request that the Examiner consider the instruction provided in M.P.E.P.

§2173.05(e), wherein the U.S. Patent & Trademark Office has clearly said,

> the failure to provide explicit antecedent basis for terms does not always render a claim indefinite. If the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite. *Ex parte Porter*, 25 USPQ2d 1144, 1145 (Bd. Pat. App. & Inter. 1992)....Inherent components of elements recited have antecedent basis in the recitation of the components themselves. For example, the limitation "the outer surface of said sphere" would not require an antecedent recitation that the sphere has an outer surface." M.P.E.P. §2173.05(e).

As a first point, it is noted that the scope of the claims "would be reasonably ascertainable by those skilled in the art." As such, the claims are not indefinite. As a second point, all of the above indicated terms regard inherent features of the recited elements; as such antecedent basis is provided in the recitation of the features themselves. However, in an effort to expedite the allowance of the claims, the indicated terms have been amended as believed to be desired by the Examiner. These amendments in no way change the scope of the claims as adequate antecedent basis and clarity was present in the claims prior to amendment. Withdrawal of the rejections is therefore respectfully requested.

Claim 31 has been amended for lacking antecedent basis for the term "said flow matrix." Claim 31 has been amended to correct the error in the claim dependency and to have claim 31 properly depend

from claim 12. Withdrawal of the rejection is therefore respectfully requested.

Claim 5 has been rejected as being "unclear if the receptor-binding capacity of the solid phase is directed to the same target as the solid phase binding capacity of receptor contacted with the sample." Applicants traverse this rejection and withdrawal thereof is respectfully requested. Claim 5 recites,

> 5. The method according to claim 4, wherein all of the receptor contacted with the sample has reactivity towards said binding sites on the solid phase, and receptor-binding capacity of the solid phase is less than solid-phase binding capacity of receptor contacted with the sample.

Claim 5 clearly states the following properties associated with elements of the claim,

a) "all of the receptor contacted with the sample has reactivity towards said binding sites on the solid phase" Thus, 100% of the receptor has the ability to bind to the binding sites of the solid phase.

b) "receptor-binding capacity of the solid phase is less than solid-phase binding capacity of receptor contacted with the sample" This statement simply means that the capacity of the receptor to bind to the solid phase is in excess compared to the binding capacity of the solid phase.

Applicants believe that claim 5 as currently drafted clearly defines the invention and that the above comments supplement that clarity. As stated under M.P.E.P. §2173.02, "some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire." However, is the Examiner is still of the position that claim 5 is unclear, the Examiner is requested as further suggested in M.P.E.P. §2173.02 "to suggest claim language to applicants to improve the clarity or precision of the language used."

Rejections under 35 U.S.C.§102(b)

The Examiner maintains the rejection of claims 1, 4, 6-8, 10, 13, 14, 15, 22, 25 and 28 under 35 U.S.C. §102(b) as being anticipated by either EP 0105714 (hereinafter referred to as "EP '714"). The Examiner further maintains the rejection of claims 1-3, 8-10, 13, 14, 16 and 17 under 35 U.S.C. §102(b) as being anticipated by US 6,184,042 (hereinafter referred to as U.S. '042").

Applicants traverse these rejections and withdrawal thereof is respectfully requested. "To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention,

either explicitly or inherently." In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997).

In response to Applicants arguments of November 14, 2002 the Examiner asserts the following points in finding the arguments insufficient to distinguish from the references.

1) The Examiner asserts that recitation of "comprising" would include other components including a mixture of bound and free receptor. Applicants disagree with this interpretation of the claims by the Examiner. Under M.P.E.P. §2111, the Examiner is required to examine the claims such that 'the pending claims must be "given the broadest reasonable interpretation consistent with the specification."' The Examiner's interpretation of the claims would be inconsistent with the disclosure in the specification.

2) The Examiner further asserts that recitation of "comprising" allows the claim steps to be carried out in any order. As noted above, the claims are required to be given the broadest reasonable interpretation consistent with the specification. The determination of whether or not steps of a claim must be done in the recited order is not determined whether the transitional language of the claim is "comprising" as does present claim 1. The Examiner is directed to Mantech Environmental Corp. v. Hudson Environmental Services Inc., wherein the Court of Appeals for the Federal Circuit held that the sequential nature of steps in a claim

are determined by the plain meaning of the claim and the written description in the specification. Mantech Environmental Corp. v. Hudson Environmental Services Inc., 47USPQ2d 1732 (Fed. Cir. 1998). In Mantech the claim in question recited in part,

> 1. A method for remediating a hydrocarbon-contaminated region of a subterranean body of groundwater to destroy or reduce the initial concentration levels of hydrocarbon contaminants, **comprising** the steps of:
> (a) providing a plurality of mutually spaced wells intersecting said groundwater region;
> (b) providing a treating flow of acetic acid from one or more of said wells into said groundwater region, to establish acidic conditions therein...(emphasis added)

Thus, the claim in question in Mantech recited the open transitional language of "comprising." However, the Federal Circuit found that based on the plain meaning of the claim that step (b) could not be carried out until step (a) was performed, i.e. it would not be possible to provide "a treating flow of acetic acid from one or more of said wells" unless the wells were first provided. Thus, the claim of Mantech was interpreted as requiring that the recited steps be carried out sequentially.

The present invention of claim 1 recites in steps (a) and (b):

> a) contacting the sample with an amount of a receptor which binds specifically to the analyte to form an analyte/receptor complex, and which is in excess of that required to bind all analyte in the sample,
> b) isolating on a solid phase a fraction of receptor contacted with the analyte, including analyte/receptor complex and unreacted receptor, such that the ratio between said isolated fraction of receptor and receptor

contacted with the sample is in a range of from about 1:2 to about 1:1000,

The plain meaning of the claims would require that the steps be done sequentially. It is not physically possible to isolate "a solid phase a fraction of receptor contacted with the analyte, including analyte/receptor complex and unreacted receptor, such that the ratio between said isolated fraction of receptor and receptor contacted with the sample is in a range of from about 1:2 to about 1:1000," unless the sample has been first contacted with the receptor. Thus, contrary the assertion of the Examiner the present invention is distinguished from the references, which disclose only "one-step" assays, with the sequential nature of the steps.

3) Finally, the Examiner asserts that it is unclear what is meant by "specified fraction" and that as such, the invention reads on the references. Claim 1 has been amended to define the isolated fraction of receptor such that the ratio between said isolated fraction of receptor and receptor contacted with the sample is in a range of from about 1:2 to about 1:1000. Applicants believe the invention patentable without this feature for the reasons discussed above in Points 1) and 2). However, the recitation of "isolating on a solid phase a fraction of receptor contacted with the analyte, including analyte/receptor complex and unreacted receptor, such

that the ratio between said isolated fraction of receptor and receptor contacted with the sample is in a range of from about 1:2 to about 1:1000" further distinguishes the invention from the references.

Rejections under 35 U.S.C. §103

The Examiner maintains the rejection of claim 11 and 12 under 35 U.S.C. §103 as being obvious over U.S. '042 combined with U.S. Pat. No. 6,319,676 (hereinafter referred to as "U.S. '676"). U.S. '676 is asserted to teach a lateral flow matrix using a sandwich technique in which receptors are immobilized in the reaction zone of the flow matrix.

The Examiner further maintains the rejection of claim 18 under 35 U.S.C. §103 as being obvious over U.S. '042 combined with U.S. Pat. No. 6,316,205 (hereinafter referred to as "U.S. '205") and claims 19-28 and 33-38 as being obvious over U.S. '042 and U.S. '676 combined with U.S. Pat. No. 5,420,016 (hereinafter referred to as "U.S. '016"). U.S. '016 is asserted to teach the assembly of components into a test kit.

Applicants traverse these rejections and withdrawal thereof is respectfully requested. As discussed above, the present invention is distinguished from the primary references in the features of 1) using only one receptor type; 2) the sequential binding of affinity

reagents; and 3) the isolation on a solid phase a fraction of receptor contacted with the analyte, including analyte/receptor complex and unreacted receptor, such that the ratio between said isolated fraction of receptor and receptor contacted with the sample is in a range of from about 1:2 to about 1:1000.

There is no disclosure in any of the secondary references of these three features of the present invention. As such, combining the secondary references of U.S. '676, U.S. '205 or U.S. '016 with the teachings of the primary references will not achieve the invention. In addition, the present invention has the advantageous property of improved results with lateral flow assays on high concentration samples. As such, the present invention is not obvious over the cited prior art references and withdrawal of the rejections is respectfully requested.

A marked-up version of the claims showing all changes is attached hereto.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, Ph.D. (Reg. 40,069) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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MARKED-UP VERSION SHOWING CHANGES

IN THE CLAIMS

Claims 11, 20, 23 and 26 have been cancelled without prejudice or disclaimer of the subject matter contained therein.

Claims 1, 4, 6-7, 12, 19, 21, 22, 24, 25, 27, 28, 31, and 33-38 have been amended as follows.

1. (Thrice Amended) A method of determining an analyte in a sample comprising the steps of:

a) contacting the sample with an amount of a receptor which binds specifically to the analyte to form an analyte/receptor complex, and which is in excess of that required to bind all analyte in the sample,

b) isolating on a solid phase a ~~specified~~ fraction of receptor contacted with the analyte, including analyte/receptor complex and unreacted receptor, **such that the ratio between said isolated fraction of receptor and receptor contacted with the sample is in a range of from about 1:2 to about 1:1000**,

c) detecting the amount of analyte/receptor complex in said isolated ~~specified~~ fraction, and

d) from the detected amount of analyte/receptor complex, determining the concentration of analyte in the sample.

4. (Thrice Amended) The method according to claim 1 or 2, wherein isolating said ~~specified~~ fraction of receptor contacted with the sample on the solid phase comprises providing a solid phase having binding sites incorporated thereon for the receptor, and after contacting the sample, or an aliquot thereof, with a liquid phase containing the receptor, binding said ~~specified~~ fraction of receptor to the solid phase.

6. (Amended) The method according to claim 4, wherein only ~~a specified fraction~~ **the ratio between the total binding capacity** of receptor ~~contacted with the sample has reactivity~~ **and binding capacity of receptor** towards said binding sites on the solid phase **is in the range of from about 2:1 to 1000:1**.

7. (Twice Amended) The method according to claim 1 or 2, wherein isolating said ~~specified~~ fraction of receptor on the solid phase comprises contacting the sample with ~~a specified amount of~~ receptor, ~~a specified fraction of which amount~~ **wherein a minor fraction of said receptor** is immobilized to said solid phase and the remaining amount of receptor being in a liquid phase.

12. (Twice Amended) The method according to claim 1, wherein said solid phase binding sites for the receptor are immobilized in a reaction zone of **a** flow matrix.

19. (Twice Amended) A test kit for determining an analyte in a sample, comprising ~~a specified amount of~~ a receptor reagent having a first part which binds specifically to the analyte, and a solid phase member having immobilized thereon a ligand which binds specifically to a second part of the receptor, wherein receptor-binding capacity of said ligand immobilized on the solid phase member is less than ligand-binding capacity of said ~~specified amount of~~ receptor reagent**, and wherein the ratio between receptor-binding capacity of ligand immobilized on the solid phase and ligand-binding capacity of the analyte-specific receptor reagent is in the range of from about 1:2 to about 1:1000**.

21. (Trice Amended) The test kit according to claim 19 ~~or 20~~, further comprising a lateral flow membrane strip having said receptor-binding ligand immobilized in or on a reaction zone of the membrane and having said analyte-binding receptor reagent dissolvably pre-deposited in or on the membrane upstream of the reaction zone.

22. (Twice Amended) A test kit for determining an analyte in a sample, comprising ~~a specified amount of~~ a receptor reagent having a first part which binds specifically to the analyte, wherein only a ~~specified~~ fraction of receptor reagent has a second part which binds to a specific ligand, and a solid phase member having said specific ligand immobilized thereon**, such that the ratio between ligand-binding analyte-specific receptor and analyte-specific receptor is in a range of from about 1:2 to about 1:1000**.

24. (Trice Amended) The test kit according to claim 22 ~~or 23~~, further comprising a lateral flow membrane strip having said receptor-binding ligand immobilized in or on a reaction zone of the membrane and having said analyte-binding receptor reagent dissolvably pre-deposited in or on the membrane upstream of the reaction zone.

25. (Twice Amended) A test kit for determining an analyte in a sample, comprising ~~a first specified amount of~~ an analyte-binding receptor reagent, and a solid phase member having immobilized thereon ~~a second specified amount of~~ said analyte-binding receptor reagent**, wherein the ratio between said second amount of analyte-binding receptor reagent immobilized to the solid phase, and said**

first and second amounts of analyte-binding receptor reagent together is in range of from about 1:2 to about 1:1000.

27. (Amended) The test kit according to claim 25 ~~or 26~~, comprising a lateral flow membrane strip having a second amount of analyte-binding receptor immobilized in or on a reaction zone of the membrane and having said first amount of analyte-binding receptor dissolvably pre-deposited in or on the membrane upstream of the reaction zone.

28. (Amended) The test kit according to claim 25 ~~or 26~~, comprising a solid phase well having said amount of analyte binding receptor immobilized therein and having said first amount of analyte-binding receptor dissolvably pre-deposited in the well or in close contact with the well.

31. (Amended) The method according to claim **12** ~~10~~, wherein said flow matrix is a lateral flow matrix.

33. (Twice Amended) The test kit according to claim **19** ~~20~~, wherein the ratio between ~~the~~ receptor-binding capacity of ligand immobilized on the solid phase and ~~the~~ ligand-binding capacity of

the analyte-specific receptor reagent is in **a** ~~the~~ range of from about 1:5 to 1:100.

34. (Twice Amended) The test kit according to claim **19** ~~20~~, wherein the ratio between ~~the~~ receptor-binding capacity of ligand immobilized on the solid phase and ~~the~~ ligand-binding capacity of the analyte-specific receptor reagent is no more than about 1:20.

35. (Twice Amended) The test kit according to claim **22** ~~23~~, wherein the ratio between ligand-binding analyte-specific receptor and analyte-specific receptor is in ~~the~~ **a** range of from about 1:5 to 1:100.

36. (Twice Amended) The test kit according to claim **22** ~~23~~, wherein the ratio between ligand-binding analyte-specific receptor and analyte-specific receptor is no more than about 1:20.

37. (Twice Amended) The test kit according to claim **25** ~~26~~, wherein the ratio between said ~~second amount of~~ analyte-binding receptor substance immobilized to the solid phase, and ~~said first and second amounts of~~ **total** analyte-binding receptor reagent **in said kit** ~~together~~ is in ~~the~~ **a** range of from about 1:5 to 1:100.

38. (Twice Amended) The test kit according to claim **25** ~~26~~, wherein the ratio between said ~~second amount of~~ analyte-binding receptor substance immobilized to the solid phase, and ~~said first and second amounts of~~ **total** analyte-binding receptor reagent ~~together~~ **in said test kit** is no more than about 1:20.